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I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO: ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231, ON THE DATE INDICATED BELOW.

BY: Helene Gabel DATE: March 9, 2000

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Patent Application of Louis S. Kucera *et al.*	: Group Art Unit: 1611
Appln. No.:	09/412,539	: Examiner: Brenda Coleman
Filed:	**October 4, 1999 (Correct)** October 5, 1999 (Incorrect)	: Attorney Docket : No. **00443-17U3**
For:	LIPID ANALOGS FOR TREATING VIRAL INFECTIONS	: (200443.0064) : (WFU 9503)

RESPONSE TO RESTRICTION REQUIREMENT

In response to the Office Action dated January 12, 2000 (Paper No. 4) containing the Examiner's Restriction Requirement in the above-referenced application, Applicants respectfully submit the following Response to Restriction Requirement. This Response to Restriction Requirement is timely filed in view of the accompanying Petition for a one-month extension of time extending the time for a response to the Restriction Requirement to and including March 12, 2000.

The Examiner has required restriction of claims 20-33, 39-44, 50-55, 88-94 and 100 (Group I), drawn to compounds and method of use of compounds of formula II, claims 56-71, 95-96 and 101 (Group II), drawn to compounds and method of use of compounds of formula III wherein B is purine, claims 56-71, 95-96 and 101 (Group III), drawn to compounds and method of use of compounds of formula III wherein B is pyrimidine, claims 72-81, 97-98 and 102 (Group IV), drawn to compounds and method of use of compounds of formula IV wherein B is purine, and claims 72-81, 97-98 and 102 (Group V), drawn to compounds and method of use of compounds of formula IV wherein B is pyrimidine. The Examiner argues that the inventions defined by Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1

and that the claims are drawn to several independent and distinct structural formulae (*i.e.*, formulae II-IV) which lack a common chemical structure.

As a first matter, Applicants do not understand why the Examiner is applying a PCT rule standard to a U.S. application. Nevertheless, Applicants hereby respond to the Restriction Requirement as if the Examiner had applied 37 C.F.R. § 1.142, the appropriate U.S. rule for this application.

Claims 20-33, 39-44, 50-55, 72-81, 88-94, 97-98, 100 and 102 (the claims constituting Groups I, IV and V) have been cancelled in the accompanying Preliminary Amendment. Thus, the Examiner's Restriction Requirement with regard to the claims of Groups I, IV and V is moot. Applicants therefore only address herein the Restriction Requirement with respect to Groups II and III.

Traversal of Restriction Requirement

Applicants respectfully traverse the Examiner's Restriction Requirement because the chemical and biological properties of the compounds of Groups II and III are not patentably distinct, and relate to a single, general inventive concept having a common chemical structure and the same chemical formula (formula III). Since Applicants have cancelled the invention defined by the claims of Groups I, IV and V from consideration, the only compounds under consideration in the present Restriction Requirement are the compounds encompassed by the inventions defined by the claims of Groups II and III, comprising the subject matter of claims 56-71, 95-96 and 101, directed to compounds and methods of use of compounds having structural formula III.

The Examiner opines that compounds of Groups II and III lack a common chemical structure and are thus patentably distinct. Applicants respectfully content that this assertion is factually incorrect. The compounds of the claims of Groups II and III contain identical phospholipid backbones composed of the same three carbon backbone with a phosphate group at the C-3 position which is covalently linked via a phosphonate linkage to a nucleoside moiety. The only difference between the compounds defined by the claims constituting Group II and the compounds defined by the claims constituting Group III is that in the nucleoside moiety

of the compounds of Group II, B is purine, whereas in the nucleoside moiety of the compounds of Group III, B is pyrimidine. Groups II and III are both defined by formula III.

Applicants respectfully submit that the variation from a purine to a pyrimidine as moiety "B" in formula III of the inventive compounds cannot properly be viewed as defining patentably distinct inventions for the reasons which follow.

Purines and pyrimidines are commonly occurring heterocyclic nitrogenous bases which are fundamental biochemical building blocks in living systems. For example, purine or pyrimidine containing nucleotides (nucleosides covalently linked to a phosphate moiety) are the monomeric units which form the polymeric nucleic acid molecules of living organisms. Since both purines and pyrimidines are commonly found building blocks of living systems, they are used interchangeably in the design of anti-viral compounds which function as analogs to naturally occuring molecules. For example, both purine (e.g. acycloguanosine) and pyrimidine (e.g. azidothymidine {AZT}, thiacytidine, 3TC and dideoxycytidine) nucleoside analogs are commonly and effectively employed as anti-viral compounds.

Moreover, the purine and pyrimidine containing variants of the nucleosides in formula III have very similar biological properties. For example, the purine dideoxyinosine (ddI) and the pyrimidine (azidothymidine, AZT) containing variants of Formula III have very similar anti-HIV-1 activities in that they both inhibit the reverse transcriptase activity of the virus, are both efficacious in the treatment of HIV-1 infection, and both exhibit similar toxicity profiles in major organ systems including bone marrow.

Since purine and pyrimidine moieties are commonly employed interchangeably in the art of preparing nucleoside analogs and can be employed interchangeably in nucleosides covalently attached to a phospholipid backbone in the inventive compounds, the variation from purine to pyrimidine in the nucleoside moiety of formula III represents an ordinary, non-variation in substituents having similar biological properties. In view of these several similar biological properties of the purine and pyrimidine variants of the nucleoside containing phospholipids of formula III, Applicants are not aware of any biological basis to assert that Groups II and Groups III are patentably distinct inventions.

Not only are purine and pyrimidine containing variants of formula III very similar in terms of biological properties, but they are also very similar chemically. Purine and

pyrimidine containing nucleosides are known in the art to have very similar chemical properties. For example, purine and pyrimidine variants of the nucleoside containing phospholipids of formula III have similar solubility profiles in common organic solvents such as methanol, dimethyl sulfoxide, and chloroform. Furthermore, the purine and pyrimidine variants exhibit very similar pKa values, and similar stabilities to chemical reagents and susceptibility/resistance to enzymatic attack.

Moreover, the compounds of Groups II and Groups III are both prepared by the same synthetic schemes. For example, the synthetic schemes for the preparation of both the purine and pyrimidine variants of the nucleoside containing phospholipids of formula III are described in Piantadosi et al., 1991, J. Med. Chem. 34:1408-1414; and Kucera et al., 1998, Antiviral Chemistry and Chemotherapy 9:157-165.

In view of these several very similar chemical properties of the purine and pyrimidine variants of the nucleoside containing phospholipids of formula III, Applicants are not aware of any chemical basis to assert that Groups II and Groups III are patentably distinct inventions.

Thus, for all of the reasons discussed above, Applicants respectfully submit that the Examiner's restriction of the invention into Groups II and III is improper. Applicants respectfully traverse the Restriction Requirement with respect to the pending claims in view of the accompanying Preliminary Amendment (Groups II and III), and submit that the invention as defined by claims 56-71, 95-96 and 101 does not present independent and distinct structural formulae lacking a common chemical structure. Applicants therefore respectfully request reconsideration and withdrawal of the Restriction Requirement.

Provisional Election

In the event that the Examiner maintains the Restriction Requirement, Applicants provisionally elect to prosecute the invention defined by Group III, constituting claims 56-71, 95-96 and 101, drawn to compounds and method of use of compounds of formula III, wherein B is pyrimidine, for favorable examination and early action in this application.

Reconsideration and withdrawal of the Restriction Requirement as well as favorable examination of the pending claims in this application are respectfully requested.

Respectfully submitted,

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March 9 2000 By: Kathryn Doyle
(Date)

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Enclosure: Petition for Extension of Time - 1 Month